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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/543,033	CAO ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *17 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *32-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/17/08;11/22/06;11/3/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-31 and 43 in the reply filed on November 17, 2008 is acknowledged.

Claims 32-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 17, 2008.

Claims 1-31 and 43 are pending and will be examined.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on November 17, 2008 and November 22, 2006 were filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

The information disclosure statement filed November 3, 2006 fails to comply (in part) with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because certain entries were not provided with a date (see Genbank entries C37 to C123, which have been lined through). It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with

the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Sequence Compliance - Notice to Comply

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Figure 1 includes nucleic acid sequences that are 10 or more nucleotide residues in length and require corresponding sequence identifiers (SEQ ID NOs). The individual sequences must be identified with proper sequence identifiers wherever they occur in the specification, including the figures and the text.

Applicant is given a period corresponding to the instant office action within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 43 is rejected as being vague and indefinite. The claim is directed to "determining the specificity of the compound for the VEGF untranslated region" and yet, the steps of the claim do not clearly achieve the stated goal of the method. Step a) comprises testing the compound with a panel of cells using UTRs from multiple genes. Step b) comprises detecting the reporter protein product, however the final statement that "the compound is specific for VEGF UTR if the level of reporter protein expressed from the reporter gene in the presence of the compound is not altered... relative to a previously determined reference range". It is unclear if the VEGF UTR is incorporated into the method of claim 43, and is compared side-by-side with the UTR of other gene sequences or if the potential for no change in reporter levels is due to not including the VEGF UTR in the panel of UTRs tested. Clarification is requested.

Claim Interpretation

The term "with specificity" is being given the broadest reasonable interpretation in light of the specification. The term is not explicitly defined in the specification. Instead, the term is referred to in general terms such as "The specificity of a particular compound's effect on untranslated region-dependent expression of one or more other genes (preferably, a plurality of genes) can also be determined utilizing assays well-known to one of skill in the art or described

herein" (p. 35, paragraph 254). Therefore, the term is being interpreted as reading on any degree of modulation of expression mediated by the VEGF UTR.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-5, 7, 9, 13-16, 18-19, 22, 24-26, 29 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Hyder et al. (Cancer Research. 2000, vol. 60, p. 3183-3190).

With regard to claim 1, Hyder teaches a method for identifying a compound that modulates untranslated region-dependent expression of a vascular endothelial growth factor (VEGF) gene, said method comprising:

(a) contacting a member of a library of compounds with a human cell containing a nucleic acid comprising a reporter gene operably linked to an UTR of the VEGF gene (p. 3184, where the human cells were HeLa cells; p. 3185, col. 2, where tandem copies of the 5' and 3' UTR upstream of a promoter linked to a luciferase reporter gene and the cell was contacted with ER-alpha or ER-beta and detected reporter gene expression); and

(b) detecting a reporter protein expressed from said reporter gene, wherein a compound that modulates untranslated region-dependent expression of a VEGF gene with specificity is identified if the level of reporter protein expressed from said reporter gene in the presence of a

compound is altered as compared to the level of reporter protein expressed from said reporter gene in the absence of said compound or the presence of a control (p. 3186, col. 2, where the level of the reporter protein activity is measured in the presence of the 3' UTR, the 5' UTR and without the estrogen compound, See C in Figures 5A and 5B).

With regard to claim 3, Hyder teaches an embodiment of claim 1 or 2, wherein the UTR of the VEGF gene is the 5' untranslated region (5' UTR) of a VEGF gene (p. 3185, col. 2, where tandem copies of the 5' and 3' UTR upstream of a promoter linked to a luciferase reporter gene and the cell was contacted with ER-alpha or ER-beta and detected reporter gene expression).

With regard to claim 4, Hyder teaches an embodiment of claim 3 wherein the 5' UTR of the VEGF gene is operably linked upstream of the reporter gene (p. 3185, col. 2, where tandem copies of the 5' and 3' UTR upstream of a promoter linked to a luciferase reporter gene and the cell was contacted with ER-alpha or ER-beta and detected reporter gene expression).

With regard to claim 5, Hyder teaches an embodiment of claim 1 or 2, wherein the UTR of VEGF gene is the 3' untranslated region (3' UTR) of a VEGF gene (p. 3185, col. 2, where tandem copies of the 5' and 3' UTR upstream of a promoter linked to a luciferase reporter gene and the cell was contacted with ER-alpha or ER-beta and detected reporter gene expression).

With regard to claim 7, Hyder teaches an embodiment of claim 3, wherein the nucleic acid further comprises the 3' UTR of a VEGF gene (p. 3185, col. 2, where tandem copies of the 5' and 3' UTR upstream of a promoter linked to a luciferase reporter gene and the cell was contacted with ER-alpha or ER-beta and detected reporter gene expression).

With regard to claim 13, Hyder teaches an embodiment of claim 1 or 2, wherein the reporter gene encodes firefly luciferase, renilla luciferase, click beetle luciferase, green

fluorescent protein, yellow fluorescent protein, red fluorescent protein, cyan fluorescent protein, blue fluorescent protein, beta-galactosidase, beta-glucoronidase, beta-lactamase, chloramphenicol acetyltransferase, or alkaline phosphatase (p. 3185, col. 2, where tandem copies of the 5' and 3' UTR upstream of a promoter linked to a luciferase reporter gene and the cell was contacted with ER-alpha or ER-beta and detected reporter gene expression).

With regard to claim 14-16, Hyder teaches an embodiment of claim 1, wherein said cell is stably or transiently transfected with said nucleic acid (p. 3184, where HeLa cells were transfected with plasmids comprising the UTR regions upstream of the Tk promoter and the luciferase reporter gene and with plasmids expressing ER-alpha or ER-beta).

With regard to claim 19, Hyder teaches an embodiment of claim 1, wherein the human cell is a HeLa cell or a 293 cell (p. 3184, where the human cells were HeLa cells).

With regard to claim 22, Hyder teaches an embodiment of claim 1 or 2, wherein the compound is selected from a combinatorial library of compounds comprising peptoids, random biooligomers, diversomers, vinylogous polypeptides, nonpeptidal peptidomimetics, oligocarbamates, peptidyl phosphonates, peptide nucleic acid libraries, antibody libraries, carbohydrate libraries, and small organic molecule libraries (p. 3184, 'materials and methods' where the hormones were obtained separately).

With regard to claim 24-26, Hyder teaches an embodiment of claim 1, wherein the step of contacting a library of compounds with a human cell is in an aqueous solution comprising a buffer and a combination of salts, wherein the solution mimics physiologic conditions and comprises a detergen (p. 3185, col. 2, where tandem copies of the 5' and 3' UTR upstream of a

promoter linked to a luciferase reporter gene and the cell was contacted with ER-alpha or ER-beta and detected reporter gene expression).

With regard to claim 29, Hyder teaches an embodiment of claim 1 or 2, wherein the compound directly binds to an RNA transcribed from the VEGF gene (p. 3185, col. 1, where the ER-alpha and ER-beta compounds bind directly to elements in the 5' and 3'VEGF UTRs).

With regard to claim 43, Hyder teaches an embodiment of claim 1 or 2 further comprising determining the specificity of the compound for the VEGF untranslated region (p. 3185, where the specificity of the binding of the estrogen compounds to the VEGF UTR was analyzed).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 10-12, 17, 20-21 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyder et al. (Cancer Research. 2000, vol. 60, p. 3183-3190) as applied to claims 1, 3-5, 7, 9, 13-16, 18-19, 22, 24-26, 29 and 43 above, and further in view of Levy et al. (Journal of Biological Chemistry, 1998, vol. 273, no. 11, p. 6417-6423). Hyder teaches analysis of elements in the 5' and 3' UTR of the VEGF gene which modulate expression.

With regard to claim 2, Hyder teaches a method for identifying a compound that modulates untranslated region-dependent expression of a VEGF gene, said method comprising:

(a) contacting a member of a library of compounds with a translation mixture and a nucleic acid comprising a reporter gene operably linked to an UTR of the VEGF gene (p. 3185, col. 2, where tandem copies of the 5' and 3' UTR upstream of a promoter linked to a luciferase reporter gene and the cell was contacted with ER-alpha or ER-beta and detected reporter gene expression); and (b) detecting a reporter protein expressed from said reporter gene, wherein a compound that modulates untranslated region-dependent expression of a VEGF gene with specificity is identified if the level of reporter protein expressed from said reporter gene in the presence of a compound is altered as compared to the level of reporter protein expressed from said reporter gene in the absence of said compound or the presence of a control (p. 3186, col. 2, where the level of the reporter protein activity is measured in the presence of the 3' UTR, the 5' UTR and without the estrogen compound, See C in Figures 5A and 5B).

Regarding claim 2, Hyder does not teach analysis in a cell free system.

With regard to claim 2, Levy teaches analysis in a cell free system (p. 6417, 'preparation of S-100 extracts and in vitro RNA Degradation Assays with HuR and HuR antiserum).

With regard to claim 10, Levy teaches an embodiment of claim 1 or 2, wherein the UTR of the VEGF gene comprises an iron response element ("IRE"), internal ribosome entry site ("IRES"), upstream open reading frame ("uORF"), or AU-rich element ("ARE") (Figure 1, where the VEGF, regulatory segment comprises an AU rich region, highlighted in the inset of the figure; p. 6417, col. 2, where it is also noted that the protein binds to an AU-rich element in the VEGF 3' UTR).

With regard to claim 11, Levy teaches an embodiment of claim 1 or 2, wherein the nucleic acid is further polyadenylated at the 3' end (Figure 1, where the nucleic acid is polyadenylated).

With regard to claim 12, Levy teaches an embodiment of claim 1 or 2, wherein the nucleic acid is selected from the group consisting of a nucleic acid that is capped at the 5' end and a nucleic acid that is not capped at the 5' end (Figure 1, where the nucleic acid is not capped at the 5' end).

With regard to claim 17, Levy teaches an embodiment of claim 1 or 2 further comprising measuring the effect of said compound on the expression of the VEGF gene (Figure 5 and 6, where the Western blot shows expression analysis of the VEGF gene).

With regard to claim 20, Levy teaches an embodiment of claim 3, wherein the cell-free translation mixture is a cell extract (p. 6418, col. 2, where cell free extracts from 293T clones were analyzed with HuR affinity purified antiserum).

With regard to claim 21, Levy teaches an embodiment of claim 20, wherein the cell extract is derived from is a human cell, a yeast cell, a mouse cell, a rat cell, a Chinese hamster ovary ("CHO") cell, a Xenopus oocyte, a MCF-7 cell, a primary cell, an undifferentiated cancer cell, a reticulocyte, or a rye embryo (p. 6418, col. 2, where cell free extracts from 293T clones were analyzed with HuR affinity purified antiserum).

With regard to claim 30, Levy teaches an embodiment of claim 1 or 2, wherein the compound binds to one or more proteins that modulate untranslated region-dependent expression of the VEGF gene (Figure 1, where the VEGF, regulatory segment comprises an AU rich region,

highlighted in the inset of the figure; p. 6417, col. 2, where it is also noted that the protein binds to an AU-rich element in the VEGF 3' UTR).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have applied the additional VEGF targets to the reporter gene construct format described by Hyder. Levy teaches an analysis of the hypoxic stabilization of VEGF in the presence of an RNA binding protein, HuR, however, the inclusion of this format in the analysis of the control of the hypoxic stabilization, including the analysis of binding sites for the HuR protein would mesh well with the techniques described generally by Hyder.

Claims 6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyder et al. (Cancer Research. 2000, vol. 60, p. 3183-3190) as applied to claims 1, 3-5, 7, 9, 13-16, 18-19, 22, 24-26, 29 and 43 above, and further in view of Iida et al. (Life Sciences, 2002, vol. 71, p. 1607-1614). Hyder teaches analysis of elements in the 5' and 3' UTR of the VEGF gene which modulate expression.

Hyder does not teach the inclusion of the 3' UTR operably linked downstream of the reporter gene.

With regard to claim 6 and 8, Iida teaches wherein the 3' UTR of the VEGF gene is operably linked downstream of the reporter gene (Figure 1, where the 5' UTR is placed upstream of the reporter gene and the 3' UTR is placed downstream of the reporter gene).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to vary the location of the 3' UTR relative to the reporter gene in the constructs. As taught by Iida, "we examined the role of the 5' UTR and 3' UTR of VEGF gene in glucose deprived conditions using luciferase assay system. 5' UTR containing reporter vector

did not show increase of activity in glucose deprived conditions in contrast to the result in oxygen deprived conditions. Both 5' UTR and 3' UTR containing vector demonstrated significant increase of activity in glucose deficient conditions compared with 5'UTR containing vector" (Abstract). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified Hyder to include constructs with the 3' and 5' UTR in their physiological locations relative to the reporter gene in the construct.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hyder et al. (Cancer Research. 2000, vol. 60, p. 3183-3190) as applied to claims 1, 3-5, 7, 9, 13-16, 18-19, 22, 24-26, 29 and 43 above, and further in view of Benjamin et al. (PNAS, 1997, vol. 94, p. 8761-8766). Hyder teaches analysis of elements in the 5' and 3' UTR of the VEGF gene which modulate expression.

Hyder teachs all of the limitations of claims 1, 3-5, 7, 9, 13-16, 18-19, 22, 24-26, 29 and 43 as recited in the 102 rejection stated above. However, Hyder does not teach that the reporter gene is the ORF of the VEGF gene (Abstract).

With regard to claim 9, Benjamin teaches an embodiment of claim 1 or 2, wherein the reporter gene is the open reading frame (ORF) of the VEGF gene and optionally further comprises an intron (p. 8761, col. 2, 'materials and methods', where the pTET-VEGF construct comprises the full-length coding sequence of mouse VEGF165 amplified by PCR from a VEGF cDNA clone).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Hyder to incorporate the ORF of VEGF as taught by Benjamin to arrive at the claimed invention with a reasonable expectation for success.

As taught by Benjamin, "the full-length coding sequence of mouse VEGF165 amplified by PCR from a VEGF cDNA clone". Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have adjusted the teachings of Hyder to incorporate the ORF of VEGF as taught by Benjamin to arrive at the claimed invention with a reasonable expectation for success.

Claims 23, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyder et al. (Cancer Research. 2000, vol. 60, p. 3183-3190) as applied to claims 1, 3-5, 7, 9, 13-16, 18-19, 22, 24-26, 29 and 43 above, and further in view of Cho et al. (Expert Opin Ther Targets, 2002, vol. 6, no. 6, p. 679-689). Hyder teaches analysis of elements in the 5' and 3' UTR of the VEGF gene which modulate expression.

Hyder does not teach small organic molecule libraries.

With regard to claim 23, Cho teaches an embodiment of claim 22, wherein the small organic molecule libraries are libraries of benzodiazepines, isoprenoids, thiazolidinones, metathiazanones, pyrrolidines, morpholino compounds, or diazepindiones (Table 2, where a variety of compounds useful in treatment are listed).

With regard to claim 27, Cho teaches an embodiment of claim 1 or 2 further-comprising (c) determining the structure of the compound that modulates untranslated region-dependent expression of the VEGF gene (Figure 8, where in a library where the small molecule comprises a protein, the structure can be determined using mass spectrometry).

With regard to claim 28, Cho teaches an embodiment of claim 27, wherein the structure of the compound is determined by mass spectroscopy, NMR, vibrational spectroscopy, or X-ray

crystallography (Figure 8, where in a library where the small molecule comprises a protein, the structure can be determined using mass spectrometry).

It would have been prima facie obvious to one of ordinary skill to include a rationally designed target library in the screening for compounds which modulate expression of VEGF, particularly as controlled or mediated by the 5' or 3' UTR of the VEGF gene. Cho teaches "proteomics analyzes differentially regulated proteins, elucidates protein structure and function, and indentifies interacting partners" (p. 684). Cho also teaches "the most common method in proteome analysis is to perform a 2D gel electrophoresis (2-DE) on a protein sample preparation isolated from a defined set of conditions (i.e. normal versus diseased and control versus drug-treated). Protein bands of interest are digested and identified using mass spectrometry (See Figure 8)" (p. 686). Therefore, it would have been obvious to one of ordinary skill to include a rationally designed target library in the screening for compounds which modulate expression of VEGF, particularly as controlled or mediated by the 5' or 3' UTR of the VEGF gene

Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hyder et al. (Cancer Research. 2000, vol. 60, p. 3183-3190) as applied to claims 1, 3-5, 7, 9, 13-16, 18-19, 22, 24-26, 29 and 43 above, and further in view of Eibl et al. (Plant Journal, 1999, 19(3):333-345). Hyder teaches analysis of elements in the 5' and 3' UTR of the VEGF gene which modulate expression.

With regard to claim 43, Hyder teaches an embodiment of claims 1 or 2, comprising determining the specificity of the compound for the VEGF UTR by contacting the compound with a panel of cells (p. 3184, where the human cells were HeLa cells; p. 3185, col. 2, where tandem copies of the 5' and 3' UTR upstream of a promoter linked to a luciferase reporter gene

and the cell was contacted with ER-alpha or ER-beta and detected reporter gene expression).

Hyder does not teach that different genes are tested together for specificity (Abstract). With regard to claim 43, Eibl teaches an embodiment of claims 1 or 2, comprising determining the specificity of the compound for the untranslated region by (a) contacting the compound with a panel of cells, each cell in the panel isolated from each other and each cell containing a nucleic acid comprising a reporter gene operably linked to a UTR of a different gene (see abstract, where the reporter gene fusions were used to study the function of the psbA, rbcL and rpl32 UTRs in vivo; see also p. 334 and discussion); and (b) detecting a reporter gene protein expressed from the reporter gene, wherein the compound is specific for the UTR if the level of reporter protein expressed from the reporter gene in the presence of the compound is not altered or is not substantially altered relative to a previously determined reference range, or the level of reporter protein expressed from the reporter gene in the absence of the compound or the presence of a control (see abstract, where the reporter gene fusions were used to study the function of the psbA, rbcL and rpl32 UTRs in vivo; see also p. 334 and discussion).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Hyder to incorporate the test of VEGF UTR specificity as taught by Eibl to arrive at the claimed invention with a reasonable expectation for success. As taught by Eibl, "The main goal of our transformation experiments was to test if and how isolated 5' and 3' UTR sequences confer regulation of mRNA stability and translation efficiency to a neutral reporter gene (uidA) (p. 334, col. 2)". Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have

adjusted the teachings of Hyder to incorporate the ORF of VEGF as taught by Benjamin to arrive at the claimed invention with a reasonable expectation for success.

Conclusion

Claim 31 is free of the art because the prior art does not teach or reasonably suggest a compound which disrupts an interaction between the 5' UTR and the 3' UTR of the VEGF gene. The closest art of record teaches elements which bind to either the 5' or 3' UTR of the VEGF gene and even elements that include binding sites in both, however there was no apparent evidence of a compound which disrupted an interaction between the 5' and 3' UTR of the VEGF gene.

Claim 31 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephanie K. Mummert/
Examiner, Art Unit 1637

SKM